

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
PATENT EXAMINING OPERATION

Inventor: Eric Wickstrom et al.

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Examiner: Ileana Popa

Attorney Docket No.: W1133/20008

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For: COMPOUNDS AND METHODS FOR DIAGNOSTIC IMAGING AND THERAPY

DECLARATION UNDER 37 C.F.R. § 1.132

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
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Sir:

I, Eric Wickstrom, Ph. D., a citizen of the United States of America, hereby declare and state:

1. The resume attached as Exhibit A accurately reflects my professional credentials.
2. I am a co-inventor of the subject matter described and claimed in the present application.
3. I have reviewed the application and its prosecution history including the Advisory Office Action of April 19, 2007.
4. I understand from my review of the Office Action of November 14, 2006 that claims of the present application were rejected under 35 U.S.C. 103 as obvious over Tomalia et al. (U. S. Patent No. 5,714,166) in view of Meade et al. (US Patent No. 6,713,046). I understand from my attorneys that in order to establish obviousness, (1) there must be some suggestion of motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or reference when combined) must teach or suggest all the claim limitations. Also, I am informed that certain factors are relevant to obviousness rejections, including evidence of unexpected results.
5. The Examiner acknowledged on page 6 of the Office Action dated March 14, 2007 that "Tomalia et al. do not teach the specific arrangement recited in the instant claims, i.e., X-L1-P-L2-T. However, as stated above, Tomalia et al. teach all components necessary for this arrangement." I believe that for the component at issue, it is not enough to disclose single units forming the component. The order of functional units in the compound of the invention X-L1-P-

L2-T is vital to the purpose of entering a cell and binding to a nucleic acid target. As stated on page 5 of the specification:

It has now been discovered that a compound comprising a diagnostic or therapeutic moiety can be retained inside a cell by conjugating the moiety to at least one PNA that is targeted to the transcripts from one or more genes of interest. The diagnostic or therapeutic moiety is also conjugated to at least one targeting moiety specific for an extracellular receptor or other cell surface molecule. The targeting moiety binds to the surface of a cell, and the entire compound is then internalized. Once inside the cell, the PNA portion of the diagnostic or therapeutic compound binds to RNA transcripts in a sequence specific manner. Binding of the PNA to its target RNA transcript retains the compound within the cell. The PNA can be designed to bind to a predetermined nucleic acid sequence from an RNA transcript, for example a mutated or overexpressed sequence that is characteristic of a pathological state.

The compound $(T)_e(P)_x(M)_y$ taught by Tomalia et al. functions contrarily to the compound of the present invention, where it permits compound binding to multiple neighboring cells via multiple T2 interactions on the surface of the dendrimer P, preventing internalization of the compound into a single targeted cell, which in turn will prevent T1 binding to the targeted nucleic acid inside the cell.

Thus, the compound taught by Tomalia et al. fails to teach or suggest the compound of the invention. The Examiner relies on a secondary reference Meade et al for the use of Gd(III) as a contrast agent for MRI. However, the secondary reference Meade et al. does not remedy the aforementioned deficiency of the primary reference, the Tomalia et al. reference, to teach or suggest all the limitations of the base claim 1. The combination proposed by the Examiner requires the eradication of the intended function of the references. There is nothing obvious about combining references for what they do not teach. A person skilled in the art would not be motivated to employ the Tomalia compound to bind to a surface of a cell for further internalization by consequent binding of the PNA portion of the diagnostic or therapeutic compound to RNA transcripts in a sequence specific manner.

6. I understand from my review of the Office Action of November 14, 2006 that claims of the present application were rejected under 35 U.S.C. 103 as obvious over Lewis et al.

(2002) in view of Liang et al. (Molecular Therapy, 2000, 3:236-243), as evidenced by Basu et al. (1997).

7. The Examiner acknowledged that Lewis et al. “do not teach a targeting moiety capable of binding to a cell surface molecule (claim 1)” (see pages 7 and 8 of the Office Action). Interestingly, Sun et al. MicroPET imaging of MCF-7 tumors in mice via *unr* mRNA-targeted peptide nucleic acids. *Bioconjug Chem.* Mar-Apr 2005;16(2):294-305, reported an attempt to image *UNR* mRNA in human MCF7 xenografts using DO3A-Tyr-PNA-Lys₄ conjugates, a structure used previously by Lewis, et al. However, sequence-specific tumor images were not observed. The four-lysine tail at the carboxy terminus of the conjugates enabled universal cell permeation. The lack of specific tumor contrast was ascribed by the authors to uptake of the [⁶⁴Cu]PNA-Lys₄ conjugates into all cells, so that murine *unr* mRNA with the same target sequence as human *UNR* mRNA might have contributed to PET image intensities in all tissues.

8. The Liang et al. reference is relied upon to remedy the deficiency of Lewis et al. to teach the targeting moiety. Liang et al. teach construction of a transferrin-PNA conjugate associated with a plasmid DNA vector for the purpose of plasmid DNA vector delivery into cells to effect gene therapy. It is important that Liang et al. reported no cellular uptake of the transferrin-PNA:DNA conjugate until cationic polymer polyethyleneimine, associated with a plasmid DNA vector was added. Liang et al. reported enhanced vector-encoded enzymatic activity in transfected cells if transferrin-PNA was associated with the plasmid DNA vector:polyethyleneimine complex. Therefore Liang et al. provide no motivation toward the design of the present diagnostic compound without using polyethyleneimine. The toxicity of polyethyleneimine, however, teaches away from utilizing Liang et al. construct in a human. Additionally, the construct of Liang et al. lacks the specificity provided by the present invention. Transferrin is so large, its binding to its receptor is so strong, and the transferrin receptor is so ubiquitous, that all cells would take up transferrin and any other moiety conjugated to it, regardless of the presence or absence of the target nucleic acid in a cell.

9. I believe that knowledge of our invention did not exist in the prior art as the references combined by the Examiner do not disclose the problem or its source as described in the specification starting page 2, line 7 and continuing to page 4, line 25. Further, following the

cited references, one of ordinary skill in the art would have lacked motivation to use this reference to make the composition of the present invention with a reasonable expectation of success because such motivation is not present in these references; the motivation cannot be “borrowed” from current invention. The invention is directed to “methods and compounds that allow the non-invasive and effective detection of gene expression *in vivo* in a chosen cell, where the gene expression is detected with high specificity and sensitivity. The compounds should be stable, non-toxic, and should not cause degradation of mRNA expressed from the gene of interest” (page 4, lines 19-23 of the specification). Absent such reasonable motivation, the present invention would not have been obvious to a person of ordinary skill in the art in light of the references cited by the Examiner.

10. Even if the prior art creates a presumption that the present development is obvious, the Applicants have achieved surprising results which overcome this presumption. For example, we bonded an IGF1 peptide analog to the C-terminus of the chelator-PNA hybridization probes. Our successes in radioimaging of cancer gene mRNAs in breast cancer xenografts [Tian X, Aruva MR, Qin W, et al. External imaging of CCND1 cancer gene activity in experimental human breast cancer xenografts with ^{99m}Tc -peptide-peptide nucleic acid-peptide chimeras. *Journal of Nuclear Medicine*. Dec 2004;45(12):2070-2082; Tian X, Aruva MR, Qin W, et al. Noninvasive molecular imaging of *MYC* mRNA expression in human breast cancer xenografts with a [^{99m}Tc]peptide-peptide nucleic acid-peptide chimera. *Bioconjugate Chemistry*. 2005;16(1):70-79] and in pancreas cancer xenografts [Chakrabarti, A., Aruva, M. R., Sajankila, S. P., Thakur, M. L., and Wickstrom, E. (2005) Synthesis of novel PNA-peptide chimera for non-invasive imaging of cancer. *Nucleosides, Nucleotides, and Nucleic Acids* 24:409-414; Chakrabarti, A., Zhang, K., Aruva, M.R., Cardi, C.A., Opitz, A.W., Wagner, N.J., Thakur, M.L., and Wickstrom, E. (2007) *KRAS* mRNA expression in human pancreatic cancer xenografts imaged externally with [^{64}Cu]DO3A-peptide nucleic acid-peptide chimeras. *Cancer Biology & Therapy* 6(6): in press] resulted from our design of dual-specificity hybridization probes that required receptor-specific uptake, followed by mRNA-specific hybridization and retention in cancer cells. Others skilled in the art did not anticipate our design, so that our positive results were unexpected.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine and/or imprisonment under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Date: 14 May 07



Eric Wickstrom, Ph. D.

EXHIBIT A
CURRICULUM VITAE: Eric Wickstrom, Ph.D.

I. PERSONAL DATA

Title: Professor of Biochemistry & Molecular Biology

Research Interests: Genetic cancer sensing, imaging, and therapy; antibiotics bonded to medical implants

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II. EDUCATION

1964-1968: Bachelor of Sciences with Honor, Biology, California Institute of Technology,
Pasadena, California mentor: Dr. Jerome Vinograd

1968-1972: Doctor of Philosophy, Chemistry, University of California, Berkeley, California mentor:
Dr. Ignacio Tinoco

1973-1974: Research Associate, Chemistry, and Molecular, Cellular, and Developmental Biology, University of
Colorado, Boulder, Colorado mentor: Dr. Michael Yarus

III. EXPERIENCE

1974-1981: Assistant Professor of Chemistry, University of Denver, Denver, Colorado

1981-1982: Senior Research Scientist, Recombinant DNA Division, Southern Biotech, Inc., Tampa, Florida

1982-1983: Visiting Associate Professor of Chemistry, University of South Florida, Tampa, Florida

1983-1986: Assistant Professor of Chemistry, University of South Florida

1986-1992: Coordinator, Biochemistry Division, Department of Chemistry, University of South Florida

1986-1987: Assistant Professor of Chemistry, Biochemistry, and Surgery, University of South Florida

1987-1991: Associate Professor of Chemistry, Biochemistry & Molecular Biology, and Surgery, University of
South Florida

1988-1992: Member, Institute for Biomolecular Science, University of South Florida

1991-1992: Professor of Chemistry, Biochemistry & Molecular Biology, and Surgery, University of South Florida

1992-1996: Professor of Pharmacology; Member, Jefferson Cancer Institute, Jefferson Medical College, Thomas
Jefferson University, Philadelphia, Pennsylvania

1997-2002: Professor of Microbiology & Immunology; Member, Kimmel Cancer Center; Member, Cardeza
Foundation for Hematologic Research, Jefferson Medical College, Thomas Jefferson University

2002-2005: Professor of Biochemistry & Molecular Pharmacology; Member, Kimmel Cancer Center; Member,
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2005-present: Professor of Biochemistry & Molecular Biology; Member, Kimmel Cancer Center; Member,
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IV. BOOKS

1. Wickstrom, E., ed. (1998) *Clinical Trials of Genetic Therapy with Antisense DNA and DNA Vectors*, Marcel Dekker, New York, ISBN 0-8247-0085-6.
2. Wickstrom, E., ed. (1991) *Prospects for Antisense Nucleic Acid Therapy of Cancer and AIDS*, Wiley-Liss, New York, ISBN 0-471-56880-5.

V. CHAPTERS AND REVIEWS

1. Panchapakesan, B., and Wickstrom, E. (2007) Nanoscale electronic sensing of cancer cells. In Nalwa, H. S., ed., *Encyclopedia of Nanoscience and Nanotechnology*, Second Edition, American Scientific Publishers, in press.
2. Panchapakesan, B., and Wickstrom, E. (2007) Nanotechnology for sensing, imaging, and treating cancer. *Surgical Oncology Clinics of North America*, in press.
3. Tian, X., Chakrabarti, A., Amirkhanov, N., Aruva, M., Zhang, K., Cardi, C., Lai, S., Thakur, M. L., and Wickstrom, E. (2007) Receptor-mediated internalization of chelator-PNA-peptide hybridization probes for radioimaging and magnetic resonance imaging of oncogene mRNAs in tumours. *Biochemical Society Transactions* **35**(Feb):72-76.
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5. Wickstrom, E., and Thakur, M. L. (2006) Imaging cancer gene activity in patients from outside the body. *Biotechnology Healthcare* **2**(2):45-48.
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7. Efimov, V., Chakhmakhcheva, O., and Wickstrom, E. (2005) Synthesis and application of negatively charged PNA analogues. *Nucleosides, Nucleotides, and Nucleic Acids* **24**(10):1853-1874.
8. Tian, X., Chakrabarti, A., Amirkhanov, N., Aruva, M., Zhang, K., Mathew, B., Cardi, C., Qin, W., Sauter, E. R., Thakur, M. L., and Wickstrom, E. (2005) External imaging of *CCND1*, *MYC* and *KRAS* oncogene mRNAs with tumor-targeted radionuclide-PNA-peptide chimeras. In El-Deiry, W., ed., *Tumor Progression and Therapeutic Resistance, Annals of the New York Academy of Sciences*, **1059**:106-144.
9. Thakur, M. L., Tian, X., Amirkhanov, N., Chakrabarti, A., Aruva, M., Rao, P. S., Qin, W., Zhu, W., Sauter, E. R., and Wickstrom, E. (2004) The role of radiolabeled peptide nucleic acid chimeras and peptides in imaging oncogene expression. *Indian Journal of Nuclear Medicine* **19**(3):98-114.
10. Wickstrom, E., Choob, M., Urtishak, K. A., Tian, X., Sternheim, N., Archdeacon, J., Efimov, V. A., and Farber, S. A. (2004) Sequence specificity of alternating hydroxypropyl/phosphono peptide nucleic acids against zebrafish embryo mRNAs. *Journal of Drug Targeting* **12**(6):363-372.
11. Wickstrom, E., Urtishak, K. A., Choob, M., Tian, X., Sternheim, N., Cross, L. M., Rubinstein, A., and Farber, S. A. (2004) Downregulation of gene expression with negatively charged peptide nucleic acids (PNAs) in zebrafish embryos. In Detrich, W., Westerfield, M., and Zon, L., eds., *Methods in Cell Biology* **77: ZEBRAFISH: Genetics, Genomics, and Informatics, 2nd ed., Elsevier/Academic Press, San Diego, Chap. 8, 137-158.**
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13. Thakur, M. L., Tian, X., Aruva, M., Qin, W., Duffy, K., Rao, P. S., Sauter, E. R., and Wickstrom, E. (2003) Imaging oncogene mRNA with Tc-99m-PNA-peptide chimeras. *Journal of Labelled Compounds and Radiopharmaceuticals* **46**:S10-S14.
14. Tian, X., Aruva, M., Rao, P. S., Qin, W., Read, P., Sauter, E. R., Thakur, M. L., and Wickstrom, E. (2003) Imaging oncogene expression. In Cho-Chung, Y. S., Gewirtz, A. M., and Stein, C. A., eds., *Therapeutic Oligonucleotides: Antisense, RNAi, Triple Helix, DNA Decoys, and DNA Chips*, *Annals of the New York Academy of Sciences* **1002**:165-188.
15. Wickstrom, E., Thakur, M. L., and Sauter, E. R. (2003) Receptor-specific targeting with complementary peptide nucleic acids conjugated to peptide analogs and radionuclides. *International Journal of Peptide Research and Therapeutics* **10**(3/4):191-214.

16. Wickstrom, E., Sauter, E. R., Tian, X., Rao, P. S., Quin, W., and Thakur, M. L. (2002) Radiolabeled PNAs for imaging gene expression. *Brazilian Archives of Biology and Technology* 45:57-69.
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20. Wickstrom, E., ed. (1999) Special Issue - Antisense Therapeutics. In *Frontiers in Bioscience* 4, <http://www.bioscience.org/current/special/antisens.htm>
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VI. RESEARCH PAPERS

1. Opitz, A. W., Amirkhanov, N. V., Wagner, N. J., and Wickstrom, E. (2007) Internalization and efflux of fluorescent polydiamidopropanoate dendrimer PNA-peptide chimeras in pancreas cancer cells. in preparation.
2. Yakubov, L. A., Likhacheva, A. C., Mechetina, L. V., Rogachev, V. A., Bogachev, S. S., Byborodin, S. I., Petrova, N. A., Shurdov, M. A., and Wickstrom, E. (2007) Natural human gene correction by small extracellular genomic DNA fragments. in preparation.
3. Panchapakesan, B., Cesarone, G., Lu, S., Hao, N., and Wickstrom, E. (2007) Single pancreas cancer cell sensing by electrophoretically deposited single wall carbon nanotubes with adsorbed monoclonal antibodies against IGF1 receptor. in preparation.
4. Zeiger, A. R., Chen, C., Edupuganti, O. M., and Wickstrom, E. (2007) Stability of radioiodinated vancomycin covalently bonded to Ti6Al4V alloy pins. in preparation.
5. Tian, X., Aruva, M. R., Zhang, K., Zhu, W., Thakur, M. L., and Wickstrom, E. (2007) Differences in the tissue distribution and pharmacokinetics of ^{64}Cu -labeled and $^{99\text{m}}\text{Tc}$ -labeled peptide nucleic acid probes for *CCND1* mRNA in immunocompromised mice bearing breast cancer xenografts. in preparation.
6. Amirkhanov, N. V., Zhang, K., Aruva, M. R., Thakur, M. L., and Wickstrom, E. (2007) $(^{111}\text{In-DO3A})_n$ -(PDAP) m -*KRAS* PNA-peptide dendrimers for scintigraphic imaging of *KRAS* mRNA in AsPC1 pancreas cancer xenografts. in preparation.
7. Millar, H. J., Nemeth, J. A., McCabe, F. L., and Wickstrom, E. (2007) Circulating interleukin 8 as an indicator of lung cancer progression in an immunodeficient rat orthotopic human xenograft model. in preparation.
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10. Wyre, D. S., Abrams, M. T., and Wickstrom, E. (2007) Lowering *BCL2* expression with siRNA in acute lymphoblastic leukemia cells does not change glucocorticoid sensitivity. in preparation.
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13. Zhang, K., Aruva, M. R., Shanthly, N., Cardi, C. A., Patel, C. A., Rattan, S., Gregory, C., Wickstrom, E., and Thakur, M. L. (2007) Vasoactive intestinal peptide (VIP) and pituitary adenylate cyclase activating peptide (PACAP) receptor specific peptide analogues for PET imaging of breast cancer: *In vitro* / *in vivo* evaluation. submitted.
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15. Amirkhanov, N. V., Zhang, K., Aruva, M. R., Shanthly, N., Lai, S., Dimitrov, I., Lackey, J. P., Cardi, C. A., Thakur, M. L., and Wickstrom, E. (2007) $(\text{Gd-DO3A})_n$ -(PDAP) m -*KRAS* PNA-peptide MRI contrast enhancement in AsPC1 pancreas cancer xenografts. *Bioconjugate Chemistry*: under revision.
16. Tian, X., Aruva, M. R., Zhang, K., Cardi, C. A., Thakur, M. L., and Wickstrom, E. (2007) *In vivo* microPET imaging of *CCND1* mRNA in human MCF7 ER+ breast cancer xenografts with an oncogene-specific [^{64}Cu]DO3A-PNA-peptide radiohybridization probe. *Journal of Nuclear Medicine*: under revision.

17. Chakrabarti, A., Zhang, K., Aruva, M. R., Cardi, C. A., Opitz, A. W., Wagner, N. J., Thakur, M. L., and Wickstrom, E. (2007) *KRAS* mRNA expression in human pancreatic cancer xenografts imaged externally with [⁶⁴Cu]DO3A-peptide nucleic acid-peptide chimeras. *Cancer Biology & Therapy* 6(6): in press.
18. Duffy, K. T. and Wickstrom, E. (2007) Zebrafish *tp53* knockdown extends the survival of irradiated zebrafish embryos more effectively than the p53 inhibitor pifithrin- α . *Cancer Biology & Therapy* 6(5): in press.
19. Antoci, V., Jr., King, S. B., Jose, B., Parvizi, J., Zeiger, A. R., Wickstrom, E., Freeman, T. A., Composto, R. J., Ducheyne, P., Shapiro, I. M., Hickok, N. J., and Adams, C. S. (2007) Vancomycin covalently bonded to titanium alloy prevents bacterial colonization. *Journal of Orthopaedic Research* 25: Epub ahead of print.
20. Edupuganti, O. P., Antoci, V., Jr., King, S. B., Jose, B., Adams, C. S., Parvizi, J., Shapiro, I. M., Zeiger, A. R., Hickok, N. J., and Wickstrom, E. (2007) Vancomycin covalently bound to Ti6Al4V pins provides longterm inhibition of *Staphylococcus aureus* colonization. *Bioorganic & Medicinal Chemistry Letters* 17(10):2692-2696.
21. McAleer, M. F., Duffy, K. T., Davidson, W. R., Kari, G., Dicker, A. P., Rodeck, U., and Wickstrom, E. (2006) Antisense inhibition of cyclin D1 expression is equivalent to flavopiridol for radiosensitization of zebrafish embryos. *International Journal of Radiation Oncology Biology Physics* 66(2):546-551.
22. Quadros, M. R. D., Connelly, S., Kari, C., Abrams, M. T., Wickstrom, E., and Rodeck, U. (2006) EGFR-dependent downregulation of Bim in epithelial cells requires MAPK and PKC- δ activities. *Cancer Biology and Therapy* 5(5):498-504.
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VII. PATENTS

1. Wickstrom, E., and Thakur, M. L. (2003) Compounds and Methods for Diagnostic Imaging and Therapy. U.S. patent application 10/688,821.
2. Hickok, N. J., and Wickstrom, E. (2003) Advanced Biomaterials and Methods of Attaching Therapeutic Agents Thereto. U.S. patent application 10/662,261.
3. Fu, Z. F., Wickstrom, E., Dietzschold, B., and Koprowski, H. (2002) Antigenomic Oligonucleotides for Treatment of Infection by Negative-Stranded Nonsegmented RNA Viruses. U.S. patent no. 6,355,621.
4. Wickstrom, E., and Basu, S. (2001) Peptide Nucleic Acid Conjugates. U.S. patent no. 6,180,767.
5. Wickstrom, E., and Cleaver, S. H. (1999) Composition and Method for Targeted Integration into Cells. U.S. patent no. 5,958,775.
6. Wickstrom, E., and Le Bec, C. (1997) Stereospecific Solid Phase Synthesis of Oligodeoxynucleoside Alkylphosphonates by Pentavalent Grignard Coupling. U.S. patent no. 5,703,223.

VIII. RESEARCH INTERESTS

Detection, control, or suppression of oncogenes and viral genes by oligonucleotides or by nonviral vectors are the goals of this laboratory. Control of gene expression comprises the central problem of biochemistry and molecular biology. We study nucleic acid-nucleic acid and protein-nucleic acid interactions because they control replication, transcription, and translation. References are to recent publications in section VI above.

Investigators in this laboratory are currently developing oligonucleotide derivatives against oncogenes in the signal transduction pathway for use as diagnostics and therapeutics for cancers. The experimental systems being studied include the human *CCND1* oncogene, *IRS1* oncogene, *MYC* oncogene, *HER2* oncogene, *KRAS* oncogene, and *TP53* oncogene in breast cancer, ovarian cancer, pancreatic cancer, prostate cancer, colon cancer, and other solid tumors. Strongly hybridizing oligonucleotide analogs capable of surviving in the bloodstream and tissues following systemic or local administration must be synthesized and tested in animal models.

Chimeric PNA-peptides that enable receptor-mediated internalization [52] are being synthesized in order to maximize cellular uptake, nuclease resistance, and RNA hybridization, while slowing excretion. Peptides that chelate gamma-emitting ^{99m}Tc have been extended from the N-termini of peptide nucleic acids with C-terminal peptide ligands for receptor uptake [44] to permit noninvasive scintigraphic imaging of *CCND1* oncogene mRNA [16, 35] and *MYC* oncogene mRNA [16, 43] in breast cancer xenografts. Positron-emitting ⁶⁴Cu has been chelated to DO3A-PNA-peptides [38] for PET imaging of *CCND1* oncogene mRNA in breast cancer xenografts [5, 16], and *KRAS* mRNA in pancreas cancer xenografts [17]. Gadolinium dendrimer-peptide nucleic acid-peptide chimeras are being used for MRI imaging of *KRAS* mRNA in pancreas cancer xenografts [15, 28].

Short interfering RNA sequences have been found efficacious against *IRS1* oncogene in breast cancer cells [14, 23], and against *MKP1* [34], *BIM* [22, 34] and *BCL2* [10] oncogenes in acute lymphoblastic leukemia cells. Negatively charged phosphono peptide nucleic acid derivatives have been found more potent and specific than

morpholinos as antisense inhibitors of zebrafish embryonic developmental genes [41], and are being pursued for oncogene inhibition [31], radiosensitization [21], and radioprotection [9, 18].

Noninvasive detection of malignant cells is also being pursued with monoclonal antibodies adsorbed to single wall carbon nanotubes [3, 25, 26]. Treatment of transformed foci is being developed with single wall carbon nanotube sheets activated by laser light [26].

Infections that develop on medical implants inflict great damage, so that efforts are starting up to covalently bond therapeutics, such as oligonucleotides, peptides, or antibiotics to titanium and other implant materials, killing *Staphylococcus aureus* on contact [4, 19, 20, 30, 36].

IX. CURRENT EXTRAMURAL RESEARCH GRANTS (Career Total: \$12,707,813)

1. DOD DAMD-17-03-1-0713, \$2,719,724, Orthopedic Implants Engineered to Prevent Post-Operative Infection of Open Fractures, Irving Shapiro, PI, Eric Wickstrom, co-investigator, 10% effort, 01 Dec 2003-30 Nov 2007, current year direct costs: \$476,231
2. NIH 1 R01 CA109231-01, \$1,940,296, PET Imaging of Breast Cancer Using Oncogene Expression, Mathew Thakur, PI, Eric Wickstrom, co-investigator, 10% effort, 1 Apr 2005-31 Mar 2009, current year direct costs: \$253,111
3. NIH 1 R01 AR051303-01, \$2,962,697, Smart Substrates for a New Generation of Implants, Irving Shapiro, PI, Eric Wickstrom, co-investigator, 9% effort, 22 Sep 2005-31 Jul 2009, first year direct costs: \$436,886
4. NIH 1 U54 CA105008-04, \$155,000, Magnetic Resonance and Near Infrared Imaging of *KRAS* mRNA, Eric Wickstrom, PI, 17% effort, subcontract from University of Pennsylvania, Network for Translational Research in Optical Imaging, Wafik El-Deiry, PI, 1 Sep 2006-31 Aug 2007, first year direct costs: \$100,000
5. DOD BC053206, \$7,000, Curcumin-nanotube preparation for breast cancer cell treatment, Eric Wickstrom, PI, 2% effort, subcontract from Geisinger Clinic, Curcumin-combretastatin nanocells as breast cancer cytotoxic and antiangiogenic agent, Anna Reeves, PI, 1 Sep 2006-31 Aug 2007, first year direct costs: \$7,000
6. NIH 1 R24 CA83105-06, \$30,000, Molecular Biology Core, Eric Wickstrom, Core Leader, 2% effort, subcontract from University of Pennsylvania, Small Animal Imaging Resource, Jerry Glickson, PI, 1 May 2007-30 June 2009, first year direct costs: \$12,903

X. PENDING EXTRAMURAL RESEARCH GRANTS

1. Prostate Cancer Foundation, \$100,000, PET Imaging of Cancer Gene Expression in Prostate Cancer, Mathew Thakur, PI, Eric Wickstrom, co-I, 10% effort, 1 July 2007-30 June 2008, first year direct costs: \$100,000
2. DOD BC062014, \$616,122, Sensing Circulating Breast Cancer Cells, Eric Wickstrom, PI, 13% effort, 1 Jul 2007-30 Jun 2009, first year direct costs: \$250,000
3. DOD BC062173, \$775,000, Breast Cancer Gene Activity PET Imaging, Eric Wickstrom, PI, 15% effort, 1 Jul 2007-30 Jun 2009, first year direct costs: \$250,000
4. NIH 1 R01 CA132054, \$1,318,133, Antisense Nanoparticle for Early Detection of Pancreatic Cancer by Magnetic Resonance Imaging, Eric Wickstrom, PI, 10% effort, subcontract from University of Delaware, Norman Wagner, PI, 1 Dec 2007-30 Nov 2012, first year direct costs: \$154,983
5. NIH 1 R21 CA132057, \$437,190, Antibody-Nanotube Device to Detect Breast Cancer Cells in Blood, Eric Wickstrom, PI, 15% effort, 1 Dec 2007-30 Nov 2012, first year direct costs: \$135,468
6. NIH 1 R01 CA126808-01A1, \$1,950,000, Oncogenic Approaches to PET Imaging of Prostate Cancer, Mathew Thakur, PI, Eric Wickstrom, co-I, 20% effort, 1 Dec 2007-30 Nov 2012, first year direct costs: \$250,000
7. Leukemia and Lymphoma Society, \$600,000, Radiohybridization Imaging and Therapy of Mantle Cell Lymphoma, Eric Wickstrom, PI, 10% effort, 1 Oct 2007-30 Sep 2010, first year direct costs: \$180,000

XI. PLANNED EXTRAMURAL RESEARCH GRANTS

1. NIH 1 R01 CA?????-01, \$1,592,310, Breast Cancer Stratification by Radiohybridization Imaging of Oncogene Activity, Eric Wickstrom, PI, 20% effort, 1 Apr 2008-31 Mar 2013, first year direct costs: \$412,362
2. NIH 1 R01 ??????, \$2,829,609, Polyurethane Bonding to Vancomycin and Bacitracin, Eric Wickstrom, PI, 20% effort, 1 Apr 2008-31 Mar 2013, first year direct costs: \$340,851

3. NIH 1 R01 CA128900-01A1, \$2,735,055, Radiohybridization Imaging of Oncogene Activity in Pancreas Cancer, Eric Wickstrom, PI, 25% effort, 1 Jul 2008-30 Jun 2013, first year direct costs: \$332,362
4. NIH 1 R01 CA?????-01, \$3,229,573, Imaging Colorectal Cancer Metastasis, Eric Wickstrom, PI, 20% effort, 1 Jul 2008-30 Jun 2013, first year direct costs: \$397,602
5. NIH 1 R01 GM?????-01, \$1,931,368, Functions of Zebrafish *chk1* and *ate1* Orthologs, Eric Wickstrom, PI, Hideko Kaji, co-PI, 20% effort, 1 Jul 2008-30 Jun 2013, first year direct costs: \$250,000
6. NIH 1 R21 CA128380-01A1, \$739,680, Comparison of MRI with mRNA Radioimaging for Determination of Breast Mass Malignancy, Eric Wickstrom, PI, 15% effort, 1 Jul 2008-30 Jun 2010, first year direct costs: \$250,000
7. NIH 1 R21 CA?????-01, \$739,680, Pilot Study of PET Imaging of *CCND1* mRNA in BIRADS 4/5 Breast Masses, Eric Wickstrom, PI, 15% effort, 1 Jul 2008-30 Jun 2010, first year direct costs: \$250,000
8. NIH 1 R21 CA127763-01A1, \$426,250, MRI and NIRF Hybridization Probes for Mutant *KRAS* mRNA in Pancreas Cancer, Eric Wickstrom, PI, 8% effort, 1 Jul 2008-30 Jun 2010, first year direct costs: \$125,000

XII. PREVIOUS EXTRAMURAL RESEARCH GRANTS

1. DOE ER63055, \$2,694,824, Oncogene mRNA Imaging with Radionuclide-PNA-Peptides, Eric Wickstrom, PI, Mathew Thakur, Co-Investigator, 15 Sep 2000-14 Dec 2006.
2. NIH N01-CO27175, \$2,131,201, Radionuclide Imaging, Treatment, and Assessment of Cancer, Eric Wickstrom, PI, Mathew Thakur, Co-Investigator, 30 Sep 2002-30 Sep 2006
3. Panagenic International, Inc., \$5,000, Homologous Recombination Between Exogenous DNA Fragments and the Genome of MCF7 Cells, 15 Dec 2003-22 Mar 2004
4. NIH R01 CA76290, \$668,995, Site Specific Gene Insertion by Transposition, 1 Jan 1999-31 Dec 2003
5. NIH R01 CA42960, \$2,473,651, Oligonucleotide Inhibition of Cell Proliferation, 1 Apr 1987-30 Jun 2003
6. NIH R03 TW01094, \$116,094, Alkylating and Cleaving Anti-*c-MYC* DNAs for Breast Cancer, Eric Wickstrom, PI, Valentina Zarytova, Co-Investigator, 1 Jul 1999-30 Jun 2003
7. NIH S10 RR14770, \$97,226, Jefferson Shared Circular Dichroism Facility, 1 Mar 2000-28 Feb 2001
8. NIH U01 CA60139, \$3,050,509, Gene-Specific Therapy of Breast and Pancreatic Cancer, 1 Aug 1992-31 Dec 1996
9. Snow Brand Milk Products, \$27,180, Synthesis and Pharmacokinetics of Antisense DNA, 1 Sep 1995-31 Aug 1996
10. American Cancer Society DHP-105, \$200,000, Antisense DNA Therapy of *ras*-Induced Tumors in Immunocompromised Mice, 1 Jan 1994-31 Dec 1995
11. American Cancer Society RD-324, \$75,000, Antisense DNA Therapy of *ras*-Induced Tumors in Nude Mice, 1 Aug 1990-31 Dec 1991
12. Genta, Inc., \$64,000, Stereospecific Synthesis of Oligodeoxynucleoside Methylphosphonate Antisense Inhibitors, 1 Jul 1989-31 May 1990
13. American Foundation for AIDS Research 00638, \$60,000, HIV *tat* Protein Interactions with mRNA TAR Sequence, 1 Jun 1988-30 Sep 1989
14. Florida High Technology and Industry Council, \$139,108, Antisense Oligodeoxynucleoside Methylphosphonate Inhibition of Human Immunodeficiency Virus Gene Expression, 1 Apr 1988-28 Jan 1991
15. Biosearch, Inc., \$50,900, Stereospecific Synthesis of All-S Oligodeoxynucleoside Methylphosphonates, 20 Jul 1987-31 Dec 1987
16. US Army Medical Research and Development Command DAMD17-86-G-6037, \$157,939, Antisense Oligodeoxynucleotide Inhibition of AIDS Virus Gene Expression, 1 Oct 1986-31 Dec 1988
17. Leukemia Society of America, \$50,000, Antisense Oligodeoxynucleotide Inhibition of Human *c-myc* Gene Expression, 1 Oct 1986-31 Dec 1987
18. NIH R01 GM32024, \$254,163, IF3 Interactions with RNA Secondary Structure, 1 Jul 1986-30 Jun 1989
19. American Cancer Society, Florida Division, \$12,000, Oligodeoxynucleotide Inhibition of Transformed Cell Proliferation, 1 Jun 1986-31 May 1987
20. American Foundation for AIDS Research 00004, \$60,000, Antisense Oligodeoxynucleotide Inhibition of AIDS Virus *gag-pol* Gene Expression and Reverse Transcriptase Activity, 1 May 1986-30 Aug 1987

21. NIH RR01554, \$70,000, Tampa Shared Circular Dichroism Facility, 1 Aug 1983-31 Jul 1984
22. NIH R01 GM28408, \$45,431, Protein-Nucleic Acid Interactions of *Escherichia coli* Initiation Factor 3, 1 Feb 1981-31 Aug 1981
23. NIH GM27462, \$52,350, Colorado Shared Circular Dichroism Facility, 30 Sep 1979-31 Aug 1981
24. NIH R01 GM24128, \$177,591, Molecular Rulers for Ribosomes, 1 Jul 1978-30 Jun 1981
25. NSF BMS 75-17781, PCM 77-25211, and PCM 79-23471, \$100,000, Molecular Rulers for Measuring RNA Structure, 1 Sep 1976-28 Feb 1981
26. NIH R01 GM23248, \$69,096, Oligonucleotide Binding Specificity of *Escherichia coli* Initiation Factor 3, 1 Jun 1976-31 May 1978

XIII. CONFERENCE GRANTS

1. International Union of Biochemistry and Molecular Biology, \$6,000; National Institutes of Health, \$5,500; Rhône-Poulenc Rorer, \$10,000; PE Biosystems, \$2,200; Hybridon, \$2,000; Glen Research, \$2,000; Gene Tools, \$2,000; Novartis, \$2,000; Trilink Biotechnologies, \$2,000; Amersham Pharmacia Biotech, \$2,000; Berry Associates, \$1,250; Inex, \$1,324; Research Genetics, \$1,000; Annovis, \$1,000; Integrated DNA Laboratories, \$1,000; Prologo, \$1,000; Millennium Conference on Nucleic Acid Therapeutics, Clearwater Beach, Florida, 8-11 Jan 2000.
2. American Society for Pharmacology and Experimental Therapeutics, \$3,000, Symposium on Antisense Oligonucleotides at the Clinical Threshold, Pharmacology 97 Meeting, San Diego, California, 7-11 Mar 1997.
3. National Institutes of Health, \$6,000; International Union of Biochemistry, \$5,000; Amgen, \$5,000; Ciba-Geigy, \$2,000; Du Pont, \$2,000; Milligen/Bioscience, \$2,000; PharmaGenics, \$2,000; Rhône-Poulenc, \$2,000; Enzo Biochem, \$1,500; Synthecell, \$1,450; Applied Biosystems, \$1,000; Boehringer/Mannheim, \$1,000; Genta, \$1,000; Gilead, \$1,000; Glaxo, \$1,000; Hybridon, \$1,000; ICI Pharmaceuticals, \$500; Integrated DNA Technologies, \$1,000; Institute for Biomolecular Science, \$1,000; Isis, \$1,000; Pfizer, \$1,000; Sandoz, \$1,000; Boron Biologicals, \$500; Glen Research, \$500; Life Sciences, \$500; Midland Certified Reagents, \$500; Research Genetics, \$500; Synthetic Genetics, \$500; Triplex, \$500; Upjohn, \$500; ICI Pharmaceuticals, \$490; International Conference on Nucleic Acid Therapeutics, with co-PI Marvin Caruthers, Clearwater Beach, Florida, 13-17 Jan 1991.

XIV. PROFESSIONAL SOCIETIES, SERVICE, AND HONORS

Reviewer of Manuscripts for *Annals of Internal Medicine*, *Anti-Cancer Drug Design*, *Antisense and Nucleic Acid Drug Development*, *Archives of Biochemistry and Biophysics*, *Biochemical Pharmacology*, *Biochemistry*, *Bioconjugate Chemistry*, *Biomaterials*, *Bioorganic and Medicinal Chemistry Letters*, *Biopolymers*, *British Journal of Cancer*, *Cancer Communications*, *Cancer Research*, *Clinical Cancer Research*, *Experimental Cell Research*, *Journal of the American Chemical Society*, *Journal of Biochemical and Biophysical Methods*, *Journal of Cellular Biochemistry*, *Journal of Chromatography*, *Journal of Molecular Biology*, *Journal of the National Cancer Institute*, *Journal of Organic Chemistry*, *Journal of Pharmacology and Experimental Therapeutics*, *Journal of Virology*, *Molecular Cancer Therapeutics*, *Molecular and Cellular Biology*, *Molecular Medicine*, *Molecular Pharmacology*, *Nature*, *Nucleic Acids Research*, *Nucleosides Nucleotides and Nucleic Acids*, *Oligonucleotides*, *Organic Letters*, *Proceedings of the National Academy of Sciences USA*, *Science*, *Tetrahedron Letters*

2006-present: Cancer Research UK Ad Hoc Reviewer

2005-present: Member of the Oligonucleotide Therapeutics Society

2004: The Hip Society Frank Stinchfield Award for Titanium Surface with Biologic Activity Against Infection

2004-present: Editorial Board, *Biotechnology Healthcare*

2001-present: Food and Drug Administration Research Programs Ad Hoc Reviewer

2001-present: Department of Energy Ad Hoc Reviewer

2000: Organizer of the International Union of Biochemistry and Molecular Biology Millennium Conference on Nucleic Acid Therapeutics

1998-present: Member of the Joint Steering Committee for Public Policy

1998-present: Member of the National Institutes of Health Steering Committee for Therapeutic Oligonucleotides

1998-2002: Member, National Institutes of Health Experimental Therapeutics 1 Study Section
1997-present: Editorial Board, *Bioconjugate Chemistry*
1993-present: Army Breast Cancer Research Program Ad Hoc Reviewer
1992-present: American Cancer Society Ad Hoc Reviewer
1991-present: Member of the International Society for Nucleosides, Nucleotides, and Nucleic Acids
1991: Organizer of the International Union of Biochemistry Conference on Nucleic Acid Therapeutics
1990-2005: Editorial Board, *Oligonucleotides*
1989-present: National Institutes of Health Ad Hoc Reviewer
1988-present: Member of the American Association for Cancer Research
1986: Guest Researcher, Max Planck Institut für Molekulare Genetik, Berlin
1986: Guest Researcher, Clinical Pharmacology Branch, Clinical Oncology Program National Cancer Institute, Bethesda, Maryland
1984: European Molecular Biology Organization Fellow, Biochemisch Laboratorium, Rijksuniversiteit, Leiden, The Netherlands
1980-present: Member of the American Society for Biochemistry and Molecular Biology
1979-present: National Science Foundation Ad Hoc Reviewer
1973-present: Member of the American Chemical Society
1968-1971: National Science Foundation Fellow, University of California, Berkeley
1966-1968: Educational Opportunity Fund Scholar, Caltech
1965-1966: Gross Fund Scholar, Caltech

XV. TEACHING EXPERIENCE

A. Thomas Jefferson University

1. Undergraduate: none
2. Graduate: BI 515 Architectural Building Blocks; BI 522 Experimental Principles in Molecular Biology; BI 525 Genetic Information; BI 614 Protein Structure and Function; BI/PR 710,720,730 Biochemical/Pharmacological Literature Seminar; BT 411 Protein Purification and Characterization; GC 550 Foundations in Biomedical Sciences; GE 652 Molecular Basis of Cancer; PR 613 Structural Biology; TE 521 Tissue Engineering
3. Residents: Radiation Oncology Residents Lectures "Radiobiologic Basis of Human Cancer"

B. University of South Florida

1. Undergraduate: BCH 3023 Introductory Biochemistry; CHM 4970 Undergraduate Research
2. Graduate: USF: BCH 5045 Biochemistry core course; BCH 6066 General Biochemistry I, Macromolecular Metabolism; BCH 6067 General Biochemistry II, Biophysical Chemistry; CHM 6973 Thesis Research; CHM 7820 Dissertation Research

C. University of Denver

1. Undergraduate: 08-1.2 Introductory Chemistry; 08-6 Chemistry of Life; 08-10 General and Organic Chemistry for the Health Sciences; 08-11 Introductory Physiological Chemistry; 08-361 Introductory Physical Chemistry; 08-381 Biochemistry I and II; 08-382 Biochemistry Laboratory; Undergraduate Research
2. Graduate: 08-390 Special Topics: Transcription; 08-390 Special Topics: Translation; 08-480 Physical Chemistry of Biopolymers; Graduate Research

XVI. UNIVERSITY, COLLEGE, AND DEPARTMENTAL COMMITTEES

2005-present: JMC Committee on Research
2005-present: Biochemistry and Molecular Biology PhD Program Committee
2005-present: KCC Seminar Committee
2005-present: TJU Strategic Planning Working Group on Cancer and Cancer Biology
2004-present: JMC Committee on Faculty Affairs
2002-present: KCC Structural Biology and Bioinformatics Committee
2000-present: KCC Circular Dichroism Facility Committee

1997-8: TJU Animal Resources Committee
1997-present: KCC Development Therapeutics Committee
1993-present: TJU Clinical Cancer Research Review Committee
1993-2002: KCC NMR Facility Committee
1993-7: KCC Computer Committee
1993-7: KCC Structural Biology Committee
1993-6: KCC Central Equipment Committee
1993-6: KCC Translational Research Committee
1991-2: USF Institute for Biomolecular Science Advisory Committee
1986-92: USF Biochemistry Division Coordinator
1985-7, 1990-2: USF Institutional Biosafety Committee
1985-92: USF Chemistry Graduate Council
1984-6: USF Radiation Safety Committee
1984-8: USF Institute of Molecular Biology and Biotechnology
1984-8: USF Natural Sciences Biotechnology Program Committee
1984-5, 1990-1: USF Biochemistry Search Committee
1983-4: USF Chemistry Seminar Committee
1978-80: DU Chemistry Graduate Committee
1978-80: DU Library Policy Committee (Chair, 1979-80)
1975-80: DU Radiation Safety Committee (Chair, 1978-80)
1975-7: DU Chemistry Undergraduate Committee
1974-5: DU Chemistry Seminar Chair

XVII. INVITED LECTURES

1. Positron emission, magnetic resonance, and near infrared hybridization imaging of *KRAS* mRNA in pancreas cancer xenografts. Network for Translational Research in Optical Imaging Retreat, Abramson Cancer Center, University of Pennsylvania, Philadelphia, Pennsylvania, 2007.
2. Design, synthesis, and testing of mRNA hybridization probes to detect cancer gene activation from outside the body, Department of Chemistry, Temple University, Philadelphia, Pennsylvania, 2007.
3. Imaging genetic markers of cellular proliferation *in vivo*, Cancer Diabetes Metabolism Seminar, Abramson Cancer Center, University of Pennsylvania, Philadelphia, Pennsylvania, 2007.
4. Molecular design of oncogene mRNA hybridization imaging probes, Department of Radiology, University of Pennsylvania, Philadelphia, Pennsylvania, 2006.
5. SPECT, PET, and MR imaging of cancer gene mRNA in tumors. Department of Biochemistry, Temple University, Philadelphia, Pennsylvania, 2006.
6. Magnetic resonance and near infrared imaging of *KRAS* mRNA in pancreas cancer xenografts. Network for Translational Research in Optical Imaging Workshop, Cancer Imaging Program, National Cancer Institute, Bethesda, Maryland, 2006.
7. Single wall carbon nanotubes to detect or ablate breast cancer cells. Department of Electrical Engineering, University of Delaware, Newark, Delaware, 2006.
8. Receptor-mediated internalization of chelator-PNA-peptide hybridization probes for radioimaging or magnetic resonance imaging of oncogene mRNAs in tumors. Biochemical Society/Royal Society of Chemistry/Royal Pharmaceutical Society of Great Britain meeting on Cellular Delivery of Therapeutic Macromolecules, Cardiff University, Wales, 2006.
9. Imaging and targeting oncogene mRNA. Network for Translational Research in Optical Imaging Retreat, Abramson Cancer Center, University of Pennsylvania, Philadelphia, Pennsylvania, 2006.
10. Is the lump malignant or benign? PNA radioimaging of oncogene mRNAs in tumors. Frontiers in Peptide Nucleic Acid and Related Technologies Symposium, Carnegie Mellon University, Pittsburgh, Pennsylvania, 2006.
11. SPECT, PET, and MR imaging of *KRAS* oncogene mRNAs in pancreatic cancer xenografts. Department of Surgery, Thomas Jefferson University, Philadelphia, Pennsylvania, 2006.

12. Tumor diagnosis by SPECT and PET imaging of cancer gene mRNA. Penn Cancer Genetics Seminar, Department of Pediatrics, University of Pennsylvania, Philadelphia, Pennsylvania, 2005.
13. Imaging cancer gene mRNA in tumors. Distinguished Lecture in Macromolecular Therapeutics, Department of Pharmacology, University of North Carolina, Chapel Hill, North Carolina, 2005.
14. Gamma and positron imaging of oncogene mRNA inside tumors from outside the body with radionuclide-chelator-PNA-peptide chimeras. Department of Chemistry, Hunter College, City University of New York, New York, New York, 2005.
15. External imaging of oncogene mRNAs in tumors. Optical Imaging Retreat, Abramson Cancer Center, University of Pennsylvania, Philadelphia, Pennsylvania, 2005.
16. Noninvasive imaging of *KRAS* oncogene mRNAs in pancreatic cancer xenografts with [¹¹¹In]DOTA-dendrimer-PNA-peptide chimeras. Pancreas Cancer 2005: State-of-the-Art, Memorial Sloan-Kettering Cancer Center, New York, New York, 2005.
17. Radionuclide-chelator-PNA-peptides for imaging cancer gene mRNAs in tumors. Department of Chemical Engineering, University of Delaware, Newark, Delaware, 2005.
18. Hydroxypropyl/phosphono peptide nucleic acid inhibition of *ccnd1* mRNA in developing zebrafish embryos: developmental consequences of cyclin D1 reduction. 1st International Symposium on Biomolecules and Related Compounds: Chemistry, Biology and Applications, Montpellier, France, 2005.
19. Noninvasive detection of oncogene overexpression by gamma and positron imaging of mRNA in tumors. Department of Radiation Oncology, University of Pennsylvania, Philadelphia, Pennsylvania, 2005.
20. External diagnosis of oncogene activation in tumors by radioimaging. Division of Hematology/Oncology, Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, 2004.
21. External imaging of *CCND1*, *MYC* and *KRAS* oncogene mRNAs with tumor-targeted radionuclide-PNA-peptide chimeras. International Conference on Tumor Progression and Therapeutic Resistance, Philadelphia, Pennsylvania, 2004.
22. Gamma and positron imaging of oncogene mRNA inside tumors from outside the body. Department of Radiology, University of Pennsylvania, Philadelphia, Pennsylvania, 2004.
23. Peptide-PNA-radionuclide chimeras for molecular diagnosis of cancer. DOE Gene Imaging Program, Chicago, Illinois, 2004.
24. Antisense nanoparticles for imaging, treatment, and assessment of pancreatic cancer gene expression. NASA/NCI Unconventional Innovations Program, San Diego, California, 2004.
25. Peptide-PNA-radionuclide chimeras for molecular diagnosis of cancer. 5th Cambridge Symposium on Nucleic Acids Chemistry and Biology, Queens' College, Cambridge, England, 2003.
26. Zebrafish embryonic gene knockdown with alternating hydroxypropyl/phosphono peptide nucleic acids. Gordon Research Conference on Purines, Pyrimidines & Related Substances, Salve Regina University, Newport, Rhode Island, 2003.
27. Imaging oncogene expression. Sixth NIH Symposium on Therapeutic Oligonucleotides, National Cancer Institute, Bethesda, Maryland, 2002.
28. Down-regulation of zebrafish embryonic developmental genes with hydroxypropyl/phosphono peptide nucleic acids. Therapeutic Oligonucleotide Interest Group, National Cancer Institute, Bethesda, Maryland, 2002.
29. Oligonucleotide conjugates for diagnosis and therapy of cancer. School of Pharmaceutical Sciences, Beijing University, China, 2002.
30. Genetic therapy with oligonucleotides. Department of Pathology and Laboratory Medicine, University of Medicine and Dentistry of New Jersey, Newark, New Jersey, 2002.
31. Imaging oncogene mRNA in mice with Tc-99m-peptide-PNA. Department of Energy Imaging Gene Expression Workshop II, Boston, Massachusetts, 2002.
32. Oncogene mRNA imaging with Tc-99m-PNA-peptides. International Conference on RNA as Therapeutic and Genomics Target, Novosibirsk Institute of Bioorganic Chemistry, Akademgorodok, Russia, 2001.
33. Oncogene mRNA imaging with Tc-99m-PNA-peptides. Fifth NIH Symposium on Therapeutic Oligonucleotides, National Cancer Institute, Bethesda, Maryland, 2000.
34. Oligonucleotide therapy for malignancies dependent on c-MYC or K-RAS. Department of Cancer Research, Merck Research Laboratories, West Point, Pennsylvania, 2000.

35. Nonviral site-specific gene insertion. Therapeutic Oligonucleotide Interest Group, National Cancer Institute, Bethesda, Maryland, 2000.
36. Site-specific gene insertion by transposition. Millennium Conference on Nucleic Acid Therapeutics, Clearwater Beach, Florida, 2000.
37. Genetic therapy with antisense DNA and DNA vectors. Department of Medicinal Chemistry, Virginia Commonwealth University, 1999.
38. Broad spectrum oligonucleotide therapy. University of Alabama, Birmingham, 1999.
39. Site specific cleavage of RNA by antisense DNA-bleomycin A₅ conjugate. Therapeutic Oligonucleotide Interest Group, National Cancer Institute, Bethesda, Maryland, 1999.
40. Genetic therapy with antisense DNA and DNA vectors. Institute for Gene Therapy, Mount Sinai School of Medicine, New York, New York, 1999.
41. Adjuvant antisense therapy for residual disease. Fourth NIH Symposium on Therapeutic Oligonucleotides, National Cancer Institute, Bethesda, Maryland, 1999.
42. Transposon Tn7 gene insertion into an evolutionarily conserved human homolog of *Escherichia coli* attTn7. Gordon Research Conference on Nucleic Acids, Salve Regina University, Newport, Rhode Island, 1999.
43. Oncogene c-MYC as a broad spectrum target for antisense DNA cancer therapy. IBC 6th International Symposium on Oligonucleotide Therapeutics, San Diego, California, 1999.
44. Broad spectrum oligonucleotide therapy. Epigenesis, Princeton, New Jersey, 1999.
45. Antisense and antigene DNA therapy. Department of Radiation Oncology, Thomas Jefferson University, Philadelphia, Pennsylvania, 1999.
46. Genetic therapy with oligonucleotides. Jefferson Center for Biomedical Research and Agricultural Medicine, Delaware Valley College, Doylestown, Pennsylvania, 1999.
47. Repressing pathogenic genes with therapeutic oligonucleotides. Department of Radiation Oncology, Thomas Jefferson University, Philadelphia, Pennsylvania, 1998.
48. Genetic therapy with antisense DNA. Aronex Pharmaceuticals, The Woodlands, Texas, 1998.
49. Assembly and behavior of stereoregular oligodeoxynucleoside methylphosphonates. Cambridge Healthtech Institute Conference on Oligonucleotide Synthesis, San Francisco, California, 1998.
50. PNA-peptide conjugates that direct nuclear localization. Cambridge Healthtech Institute Conference on Antisense Technologies, San Francisco, California, 1998.
51. Site-specific gene insertion by transposition. Kimeragen, Newtown, Pennsylvania, 1998.
52. Genetic therapy with antisense DNA and DNA vectors. Kimeragen, Newtown, Pennsylvania, 1998.
53. Oligonucleotide combination therapy to prevent murine lymphomagenesis. Oncology Frontiers Conference, Grand Cayman, British West Indies, 1997.
54. Cell specificity and backbone dependence of oligonucleotide uptake. Workshop on Future Needs and Developments in Antisense Technology, National Heart, Lung, and Blood Institute, Bethesda, Maryland, 1997.
55. Antisense oligonucleotides at the clinical threshold. American Society for Pharmacology and Experimental Therapeutics Symposium, Pharmacology 97 Meeting, San Diego, California, 1997.
56. Differential oligonucleotide activity in cell culture versus mouse models. Ciba Foundation Symposium No. 209, Oligonucleotides as Therapeutic Agents, London, England, 1997.
57. Genetic therapy with antisense DNA. College of Pharmacy, University of Minnesota, Minneapolis, Minnesota, 1997.
58. Oligonucleotide cancer therapy in animal models. Department of Pharmacology, University of Vermont, Burlington, Vermont, 1996.
59. Antisense inhibition of lymphoma growth. Department of Pharmacology, Pennsylvania State University Medical Center, Hershey, Pennsylvania, 1996.
60. Oligonucleotide therapy of murine B-cell lymphoma. Department of Pharmaceutics, Pharmacology, and Toxicology, Philadelphia College of Pharmacy and Science, Philadelphia, Pennsylvania, 1996.
61. Antisense c-myc inhibition of lymphoma growth. First NIH Symposium on Therapeutic Oligonucleotides, National Cancer Institute, Bethesda, Maryland, 1996.
62. Antisense DNA therapy in animal tumor models. BIO '96 International Biotechnology Meeting, Philadelphia, Pennsylvania, 1996.

63. Gene-targeted oligonucleotide therapy. Mid-Atlantic Pharmacology Society Annual Meeting, Pennsylvania State University Medical Center, Hershey, Pennsylvania, 1996.
64. Gene-specific therapy of breast and pancreatic cancer. Developmental Therapeutics Program, National Cancer Institute, Frederick, Maryland, 1996.
65. Cancer therapy with antisense DNA in animal models. Department of Pharmacology and Cell Biophysics, University of Cincinnati, Cincinnati, Ohio, 1996.
66. Stereospecific synthesis and hydrogen bond strength of antisense DNA methylphosphonates. Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania, 1995.
67. Prophylactic antisense DNA therapy of *Eμ-myc* transgenic mice. Vanderbilt Cancer Center, Vanderbilt University, Nashville, Tennessee, 1995.
68. Gene-specific cancer therapy with antisense DNA. Lombardi Cancer Center, Georgetown University Medical School, Washington, District of Columbia, 1995.
69. Antisense DNA cancer therapy. H. Lee Moffitt Cancer & Research Center, Tampa, Florida, 1995.
70. Prophylactic antisense DNA therapy of *Eμ-myc* transgenic mice. Centre Nationale de la Recherche Scientifique, Conférence Internationale, Les Oligonucléotides Thérapeutiques de la Cellule à l'Homme, Seillac, France, 1995.
71. Antisense DNA therapy of Burkitt's lymphoma in transgenic mice. Department of Pediatrics, Children's Hospital of Pennsylvania, Philadelphia, Pennsylvania, 1995.
72. Gene-specific cancer therapy with antisense DNA in animal models. Department of Bioscience and Biotechnology, Drexel University, Philadelphia, Pennsylvania, 1994.
73. Stereospecific antisense DNA methylphosphonates for tumor therapy. First International Antisense Conference of Japan, Kyoto, Japan, 1994.
74. Stereochemistry and hybridization strength of antisense DNA methylphosphonates. Centre Nationale de la Recherche Scientifique, Conférence Jacques Monod, Drugs Acting on Nucleic Acids, Aussois, France, 1994.
75. Targeting genes for antisense therapy. Human Genome Sciences, Rockville, Maryland, 1994.
76. Animal models for antisense DNA therapy of cancer. Department of Pharmacology, Memorial Sloan-Kettering Cancer Center, New York, New York, 1993.
77. Antisense DNA inhibition of oncogenes in mouse models. Department of Pharmacology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, 1993.
78. Gene-specific therapy of breast and pancreatic cancer. Third Anticancer Drug Discovery and Development Symposium, San Diego, California, 1993.
79. Down-regulation of oncogene expression in mice by antisense DNA therapy. Conference on Antisense Nucleic Acids, Max-Planck-Institut für Biophysikalische Chemie, Garmisch-Partenkirchen, Germany, 1993.
80. Animal models for antisense DNA therapy of cancer. International Conference on Nucleic Acid Medical Applications, Cancun, Mexico, 1993.
81. Nucleic acid therapeutics. Castle Group, New York, New York, 1993.
82. Antisense DNA therapy for cancer. Division of Hematology/Oncology, Duke University Medical Center, Durham, North Carolina, 1993.
83. Down-regulation of oncogene expression with antisense DNA therapeutics. Department of Chemistry, Bryn Mawr College, Bryn Mawr, Pennsylvania, 1992.
84. Animal models for antisense DNA therapy of cancer. Division of Biological Sciences, University of Montana, Missoula, Montana, 1992.
85. Animal models for antisense DNA therapy of cancer. Genta, Inc., San Diego, California, 1992.
86. Down-regulation of genes with antisense DNA: backbone effects. Gordon Research Conference on Biopolymers, Salve Regina University, Newport, Rhode Island, 1992.
87. Antisense DNA inhibition of c-Ha-*ras*-induced tumorigenesis in athymic nude mice. American Association for Cancer Research and American Society for Clinical Oncology Joint Annual Meeting, San Diego, California, 1992.
88. Animal models for antisense DNA therapy of cancer. Jefferson Cancer Institute, Thomas Jefferson University, Philadelphia, Pennsylvania, 1992.

89. Antisense DNA methylphosphonates in *c-myc* transgenic mice. International Symposium on Synthetic Oligonucleotides: Problems and Frontiers of Practical Application, Moscow, USSR, 1991.
90. Antisense DNA methylphosphonate inhibition of *c-myc* gene expression in transgenic mice. American Association for Cancer Research 82nd Annual Meeting, Houston, Texas, 1991.
91. Antisense DNA methylphosphonate inhibition of *c-myc* gene expression in transgenic mice. American Cancer Society, Florida Division, 14th Annual Seminar of Cancer Research, Orlando, Florida, 1991.
92. Stereochemistry of uncharged anti-oncogene DNA derivatives. Keystone Symposium on Gene Regulation by Antisense RNA and DNA, Frisco, Colorado, 1991.
93. Ablation of oncogene activity *in vitro* and *in vivo* by antisense DNA therapy. Center for Molecular Genetics, University of California, San Diego, 1991.
94. Down-regulation of oncogene expression with antisense DNA oligomers. Division of Medicinal Chemistry and Pharmaceutics, University of Kentucky, Lexington, Kentucky, 1990.
95. Steps in the development of antisense DNA therapeutics. Department of Chemistry, Georgia State University, Atlanta, Georgia, 1990.
96. Oncogene expression down-regulated by antisense DNA. Institutionen för Tumör Biologi, Karolinska Institutet, Stockholm, Sweden, 1990.
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XVIII. CONFERENCE ABSTRACTS

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